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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,297	05/17/2005	Volker Brinkmann	TX/4-32510A	9212

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EXAMINER	
FINN, MEGHAN R	

ART UNIT	PAPER NUMBER
1614	

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04/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,297	BRINKMANN ET AL.	
	Examiner	Art Unit	
	MEGHAN FINN	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-10* is/are pending in the application.

4a) Of the above claim(s) *3,5 and 7-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of group I (claims 4, 6, and 10) and election of FTY720 as the species of formula I, in the reply filed on January 28, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The information disclosure statement filed May 17, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. EP 0627406 (AM), WO 03/02313 (AR), Cleland et al. (AS), Karliner et al. (AT), Liliom et al. (AU), Lynch et al. (BA), and Pyne et al. (BB) had no reference provided and thus were not considered.

Specification Objections

The disclosure is objected to because of the following informalities: The title is not descriptive, a suggested title would be "Method of treating heart diseases with S1P receptor agonists". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 6, and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant claims a method of treating heart failure and other heart diseases comprising administering a S1P receptor agonist (claim 4), with a secondary agent such as a β-blocker (claim 6) and applicant has elected FTY720 as the specific S1P receptor agonist (claim 10). However, applicant has never shown that any of the drugs claimed, S1P receptor agonists, secondary agents, or FTY720 have any actual effect on heart diseases such as heart failure or myocardial infarction.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those

in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

There is a great deal of experimentation necessary in order to use the invention as claimed to treat heart disease (1) due to the complete lack of direction (2) and the only example that is presented merely states that "a compound of formula I" is given to rabbits and "a beneficial effect on heart failure" is observed. This example fails to enable the claims because it is not known which compound was tested, or what effects were observed. Furthermore, secondary agents were never mentioned at all. (3) The nature of the invention is treatment of humans with heart failure (4) which is a complicated art (7) and while one of skill in the art is high (6) the state of the prior art is such that the elected compound FTY720 is not even known to be a S1P receptor agonist (5) and the breath of the claims is large due to claim 4 being limited only to "a S1P receptor agonist" and claim 6 claiming a long list of co-agents (8).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 6, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 4, applicant claims a method of treating heart failure, arrhythmia, acute myocardial infarction, complications from cardiac surgery, or "improving heart energy

efficiency". It is not clear what is meant by "improving heart energy efficiency" and one of skill in the art would not know whether increasing blood flow would qualify, and applicant also claims "increasing cardiac output" which could be the same thing, however it is not clear what is meant by "improving heart energy efficiency". Claims 6 and 10 are dependent from claim 4 and thus claims 4, 6, and 10 are indefinite for failing to point out and distinctly claim the subject matter to which applicant regards as the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 4 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Baenteli et al. (US 2002/0037895 A1).

In claim 4, applicant claims a method of treating heart failure or myocardial infarction by administering a S1P receptor agonist. In claim 10, applicant specifies that the S1P receptor agonist has formula I. Applicant has elected FTY720 as the elected species of S1P receptor agonist. Baenteli et al. teaches a method of treating myocardial infarction with compounds of their formula I (page 13, [0152]) in combination with immunosuppressants such as FTY720 (page 14, [0165]). FTY720 is known in the art as an immunosuppressant, and Baenteli et al. does not teach that FTY720 is a S1P receptor agonist, however they teach the same exact compound as claimed by applicant and thus claims 4 and 10 are clearly anticipated by Baenteli et al.

Claim 4 is rejected under 35 U.S.C. 102(e) as being anticipated by Macdonald et al. (WO 02/064616).

In claim 4, applicant claims a method of treating heart failure or myocardial infarction by administering a S1P receptor agonist. Macdonald et al. teach that S1P receptor agonists are useful for treating heart failure and myocardial infarction (page 22, lines 22-27) and thus Macdonald et al. clearly anticipates claim 4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Macdonald et al. (US 2002/0037895 A1) in view of Anandasabapathy et al. (Innovative drug treatments for viral and autoimmune myocarditis).

In claim 6, applicant claims a method of treatment according to claim 4, where a second agent is co-administered with the S1P receptor agonist. Those agents are selected from a group included β-blockers and diuretics. Macdonald et al. teaches the use of S1P receptor agonists to treat heart failure and myocardial infarction (as discussed above) but fails to mention β-blockers or diuretics. It is known in the art that both β-blockers and diuretics are common treatments for heart failure and other heart related diseases. Anandasabapathy et al. teach that treatment of heart failure includes the standard regimen of diuretics, angiotensin-converting enzyme inhibitors, and β-

blockers (abstract). Thus it would have been obvious to one of ordinary skill in the art at the time of the invention that common drugs such as β-blockers and diuretics could be added to the treatment of Macdonald et al. and would be expected to achieve beneficial results. Applicant is reminded that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baenteli et al (US 2002/0037895 A1) in view of Anandasabapathy et al. (Innovative drug treatments for viral and autoimmune myocarditis).

In claim 6, applicant claims a method of treatment according to claim 4, where a second agent is co-administered with the S1P receptor agonist. Those agents are selected from a group included β-blockers and diuretics. Baenteli et al. teaches a combination therapy for treatment of myocardial infarction as discussed above, however they fail to teach β-blockers or diuretics specifically. It is known in the art that both β-blockers and diuretics are common treatments for heart failure and other heart related diseases. Anandasabapathy et al. teach that treatment of heart failure includes the standard regimen of diuretics, angiotensin-converting enzyme inhibitors, and β-blockers (abstract). Thus it would have been obvious to one of ordinary skill in the art at the time of the invention that common drugs such as β-blockers and diuretics could be added to

the treatment of Macdonald et al. and would be expected to achieve beneficial results. Applicant is reminded that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Miyamoto et al. is relevant to applicant's invention and as such is cited to show the state of the art at the time of the invention.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 7:30am-5pm Mon-Thu, 7:30am-4pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614